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PCT

COMMUNICATION OF INTERNATIONAL APPLICATIONS

(PCT Article 20)

Date of mailing:

15 November 2000 (15.11.00)

From the INTERNATIONAL BUREAU

To:

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as designated Office

The International Bureau transmits herewith copies of the international applications having the following international application numbers and international publication numbers:

International application no.:

PCT/GB00/01787

International publication no.:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

J. Zahra

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREA

From the INTERNATION	ONAL SEARCHING	AUTHORITY
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Ta:
ERIC POTTER CLARKSON
Attn. BASSETT, Richard S.
Park View House
58 The Ropewalk Communication
Nottingham NG1 500
INITED VINODOM 15
UNITED KINGDOM E 28 FC CC

ACTIONED BY:

INVITATION TO PAY ADDITIONAL FEES

26/02/2001

10/05/2000

within

30

from the above date of mailing

XXXXXXs/days

(PCT Article 17(3)(a) and Rule 40.1)

Applicant's or agent's file reference

WARM/P22402PC

International application No.

PCT/GB 00/01787

Applicant

WARNER-LAMBERT COMPANY et al.

1.	This	International	Searching	Authority
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(number of) inventions claimed in the international application covered considers that there are by the claims indicated XXXX/on the extra sheet:

Date of mailing

(day/month/year)

PAYMENT DUE

(day/month/year)

International filing date

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated Decovor the extra sheet:

will establish the international search report ((ii) X has carried out a partial international search (see Annex) on those parts of the international application which relate to the invention first mentioned in claims Nos.:

SEE ANNEX

will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

2. The applicant is hereby invited, within the time limit indicated above, to pay the amount indicated below:

GBP 572,00

GBP 5.148.00

total amount of additional fees number of additional inventions Fee per additional invention

EUR 8.505,00 EUR 945.00

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

have been found to be unsearchable under SFE ANNEX з. [х] Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2

NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,

Joannes Vergoosen

Authorized officer

Form PCT/ISA/206 (July 1992)

Fax: (+31-70) 340-3016

[N° TX/RX 6259] 01/03 '01 JEU 16:54

5771-01-MG

INVITATION TO PAY ADDITIONAL FEES

International application No.

PCT/GB 00/01787

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-2, 17, 18, 19, 30 (partial); 3, 4, 20, 21, (complete).

Pharmaceutical compositions for the treatment and prevention of sexual dysfunctions comprising compounds as disclosed in the Markush formula in claim 1.

2. Claims: 1-2,17,18,19,30 (partial), 5,22, (complete).

Pharmaceutical compositions for the treatment of anxiety, panic disorders and social phobia comprising compounds as disclosed in the Markush formula in claim 1.

3. Claims: 1-2,17,18,19,30 (partial), 6, 23 (complete).

Pharmaceutical compositions for the treatment of pulmonary hypertension comprising compounds as disclosed in the Markush formula in claim 1.

4. Claims: 1-2, 17, 18, 19, 30 (partial), 7, 24 (complete).

Pharmaceutical compositions for the treatment lung development disorders and lung repair comprising compounds as disclosed in the Markush formula in claim 1.

5. Claims: 1-2, 17, 18, 19, 30 (partial), 8, 9, 34-40 (complete).

Pharmaceutical compositions for the treatment of prostate cancer and pancreatic cancer comprising compounds as disclosed in the Markush formula in claim 1.

6. Claims: 1-2, 17, 18, 19, 30 (partial), 10, 25 (complete).

Pharmaceutical compositions for the treatment of hepatic porphyria comprising compounds as disclosed in the Markush formula in claim 1.

7. Claims: 1-2, 17, 18, 19, 30 (partial), 11, 16, 26, 29 (complete).

Pharmaceutical compositions for the treatment of visceral pain, inflammatory pain, neuropathic pain, cancer pain, postoperative pain, trigeminal neuralgia pain, acute herpetic pain, post herpetic pain, comprising compounds as disclosed in the Markush formula in claim 1.

International application No.

INVITATION TO PAY ADDITIONAL FEES

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8. Claims: 1-2,17,18,19,30 (partial), 12,13, 27 (complete).

Pharmaceutical compositions for the treatment of gastrointestinal secretory disturbances comprising compounds as disclosed in the Markush formula in claim 1.

9. Claims: 1-2,17,18,19,30 (partial), 14, 15, 28 (complete).

Pharmaceutical compositions for the treatment of emesis or anorexia comprising compounds as disclosed in the Markush formula in claim 1.

10. Claims: 10th 31-33, 41-42 (complete).

Compositions for the diagnosis of cancer comprising compounds as disclosed in the Markush formula in claim 31.

The problem to be solved by the present application is to provide pharmaceutical compositions for the treatment of diseases amenable to therapy by a bombesin receptor antagonist. These diseases are listed in the description at page 2 lines 3-9. Furthermore the inventors intend to provide compositions for the diagnosis of cancer. As solution to the above mentioned problems the inventors provide pharmaceutical compositions comprising antagonists of the bombesin receptor having the structure as shown in the Markush formula in claim

Rule 13.1 PCT deals with the requirement of unity of invention, and states the principle that an international application should relate to only one invention or, if there is more than one invention, that the inclusion of those inventions in one international application is only permitted if all inventions are so linked as to form a single general inventive concept. Rule 13.2 PCT defines the method for determining whether the requirement of unity of invention is satisfied in respect of a group of inventions claimed in an international application. Unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding "special technical features." The expression "special technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art.

The problem underlying the present application has found similar

solutions in the prior art.

W09807718 discloses bombesin receptor antagonists having the same structure of the compounds of the present application, for the treatment of depression, psychosis, affective disorders, cancer, gastrointestinal diseases and other diseases.

Bicorg. Med. Chem. Lett. VOL. 8 N. 18, Pg. 2589-2594; J. Med. Chem. 1993, 36, 2868-2877; and Eur. Journ. Chem. 1994, 29, 431-439 also disclose some of the bombesin receptor antagonists disclosed in the present application and their pharmacological properties in regard to

#283810 PAGE: 7/11

INVITATION TO PAY ADDITIONAL FEES

International application No.

PCT/GB 00/01787

some of the above mentioned diseases. The idea use to bombesin receptor antagonists for the treatment of the above mentioned diseases, is consequently known in the state of the art, and cannot serve as a single general inventive concept. In the present application no further technical feature(s) can be distinguished that can be regarded as a "special technical feature" involved in the technical relationship among the different inventions. Consequently, the present application lacks unity of invention, and the different solutions not belonging to a common inventive concept are identified as the different subjects listed above. Each of the inventions listed is a distinct invention, characterised by its own special technical feature, defining the contribution which each of the claimed inventions, considered as a whole, makes over the prior art, i.e. the use of the cited compound in relation to the treatment of each group of above mentioned diseases.

Searching these different subjects would have caused a major additional searching effort.
Only the first subject was searched.

International Application No. PCTGB 00 .01787

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Although claims 1-4, 17-21, 30 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

COMMUNICATION RELATING TO THE RESULTS OF THE PARTIAL INTERNATIONAL SEARCH

1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:

see 'Invitation to pay additional fees' 2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3.If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4.If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

Category *	ENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to daim No
E	✓WO 00 37462 A (HORWELL DAVID CHRISTOPHER ;LEWTHWAITE RUSSELL ANDREW (GB); RAPHY J) 29 June 2000 (2000-06-29) claims 1,14; examples	1-4, 18-21
A	WO 98 07718 A (HORWELL DAVID CHRISTOPHER; PRITCHARD MARTYN CLIVE (GB); WARNER LAM) 26 February 1998 (1998-02-26) cited in the application the whole document	1,2, 17-19,30
A	ASHWOOD V ET AL: "PD 176252 - The First High Affinity Non-peptide Gastrin-Releasing Peptide (BB2) Receptor Antagonist" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, GB, OXFORD, vol. 8, no. 18, 22 September 1998 (1998-09-22), pages 2589-2594, XP004138276 ISSN: 0960-894X table 3	17,30
A	✓US 5 200 408 A (BRU-MAGNIEZ NICOLE ET AL) 6 April 1993 (1993-04-06) page W	1,2, 18-20

- Special categories of cited documents:
- *A* document defining the general state of theart which is not considered to be of particular relevance
- earlier document but published on or after theinternational
- document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- document referring to an oral disclosure, use, exhibition or
- document published prior to the internationalilling date but later than the priority date claimed
- *T* fater document published after theinternational filing date or priority date and not in conflict with theapplication but cited to understand the principle or theory underlying the invention
- "X" document of particular retevance; the claimed/invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- document of particular retevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more othersuch documents, such combination being obvious to a person skilled in the at
- "&" document member of the same patent family

FOR POTASARUE (Anne) Irst sheet (July 1992)

1

ID: ERIC POTTER CLARKSON TEL NO: 0115 9552201
Annex to Form PCT/ISA/206
COMMUNICATION RELATING TO THE RESULTS
OF THE PARTIAL INTERNATIONAL SEARCH

International Application No PCT/GB 00/01787

Category *	ation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BLOMMAERT A G S ET AL: "CHOLECYSTOKININ PEPTIDOMIMETICS AS SELECTIVE CCK-B ANTAGONISTS: DESIGN, SYNTHESIS, AND IN VITRO AND IN VIVO BIOCHEMICAL PROPERTIES" JOURNAL OF MEDICINAL CHEMISTRY, 1993 XP002050616	1,2,18,
A	figure 1; table 1 VSARTORI E ET AL: "SYNTHESIS AND ANALGESIC (SITE ACTIVITIES OF UREA DERIVATIVES OF ALPHA-AMINO-N-PYRIDYL BENZENE PROPANAMIDE" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY.CHIMICA THERAPEUTICA, EDITIONS SCIENTIFIQUE ELSEVIER, PARIS, FR, vol. 29, no. 6, 1994, pages 431-439, XP000917148 ISSN: 0223-5234 tables 1-5	1,2,18,

1

15:59 MAR 01, 2001 ID: ERIC POTTER CLARKSON TEL NO: 0115 9552201

Information on patent family members

International Application No

PCT/GB 00/01787

Patent document cited in search repor	t	Publication date		atent family member(s)	Publication date
WO 0037462	А	29-06-2000	AU	2180600 A	12-07-2000
UO 0007719	Α	26-02-1998	AU	4146697 A	06-03-1998
WO 9807718	Α	20-02 1550	BR	9711342 A	17-08-1999
			EP	0920424 A	09-06-1999
			NO	990788 A	19-02-1999
			PL	331710 A	02-08-1999
			TR	9900364 T	21-05-1999
US 5200408	Α	06-04-1993	FR	2687147 A	13-08-1993

Form PCT ISA/200 (patent family annex) (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference		of Transmittal of International Search Report /220) as well as, where applicable, item 5 below.
WL-5771-PCT International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
		(22,000,000,000,000,000,000,000,000,000,
CT/GB 00/04915	20/12/2000	
pplicant		
LANDEDT COND	ANN	
ARNER - LAMBERT COMP	ANY	
This International Search Report haccording to Article 18. A copy is b	as been prepared by this International Searching Au eing transmitted to the International Bureau.	thority and is transmitted to the applicant
This International Search Report c	onsists of a total of Sheets. nied by a copy of each prior art document cited in thi	is report.
Basis of the report		
 With regard to the language in which it was file 	ge, the international search was carried out on the back, unless otherwise indicated under this item.	asis of the international application in the
the international se Authority (Rule 23.	earch was carried out on the basis of a translation of 1(b)).	the international application furnished to this
h With regard to any nucleo	tide and/or amino acid sequence disclosed in the	international application, the international search
was carried out on the bas	is of the sequence listing : ternational application in written form.	
السيا	the international application in computer readable fo	rm.
	ently to this Authority in written form.	
	ently to this Authority in computer readble form.	
the statement that	the subsequently furnished written sequence listing ation as filed has been furnished.	does not go beyond the disclosure in the
	the information recorded in computer readable form	is identical to the written sequence listing has been
2. X Certain claims we	ere found unsearchable (See Box I).	
<u></u>	is lacking (see Box II).	
,,,		
4. With regard to the title,		
the text is approve	d as submitted by the applicant.	
\overline{X} the text has been ϵ	established by this Authority to read as follows:	
NOVEL USES OF NON- AND PANIC DISORD	PEPTIDE BOMBESIN RECEPTOR ANTA ERS	GONISTS FOR TREATING ANXIETY
	•	
5. With regard to the abstract,	d as submitted by the applicant	
the text has been	d as submitted by the applicant. established, according to Rule 38.2(b), by this Autho rom the date of mailing of this international search re	rity as it appears in Box III. The applicant may, eport, submit comments to this Authority.
	pe published with the abstract is Figure No.	
as suggested by the		X None of the figures.
	cant failed to suggest a figure.	<u> </u>
<u></u>	better characterizes the invention.	

Böx I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	mational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: see FURTHER INFORMATION sheet PCT/ISA/210
2. X	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: see FURTHER INFORMATION sheet PCT/ISA/210
з. 🗌	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
	see additional sheet
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
з. 🗽	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: $1-3,8-15,20-24$
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remai	The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-3,20-23 (partially)

Use of compounds derived of urea for treating anxiety and panic disorders, social phobia.

2. Claims: 1-3,20-23 (partially)

Use of compounds derived of urea for treating pulmonary hypertension, lung repair and lung development disorder.

3. Claims: 1-3,20-23 (partially),8-14,15(partially),24

Use of compounds derived of urea for treating prostate cancer, pancreatic cancer.

4. Claims: 1-3,20-23 (partially)

Use of compounds derived of urea for treating pain of different origins.

5. Claims: 1-3,20-23 (partially), 4

Use of compounds derived of urea for treating gastrointestinal secretory disturbance.

6. Claims: 1-3,20-23 (partially)

Use of compounds derived of urea for treating hepatic porphyria.

7. Claims: 5-7,15 (partially),25

Use of compounds derived of urea for diagnostic imaging of a tumour.

8. Claims: 16-19

Method for in vitro detection of a cancer cell, which includes in vitro contacting of the cells with the compound claimed.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 20-22 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
Although claim 23 is directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Continuation of Box I.2

Present claims 1,8-15,20-24 relate to an extremely large number of possible compounds. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search for the first invention has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds described in claims 2,3.

Claims searched completely: 2-3. Claims searched incompletely: 1,8-15,20-24.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

International Application No PCT/GB 00/04915

a. classification of subject matter IPC 7 A61K31/4164 A61K31/44 A61P25/22 A61P25/24 A61K31/404 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 7 **A61K** Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, BIOSIS, CHEM ABS Data, WPI Data, PAJ, EMBASE, MEDLINE, SCISEARCH C. DOCUMENTS CONSIDERED TO BE RELEVANT Relevant to claim No. Citation of document, with indication, where appropriate, of the relevant passages Category ° 1,2, 20-23 X WO 98 07718 A (HORWELL DAVID CHRISTOPHER ;PRITCHARD MARTYN CLIVE (GB); WARNER LAM) 26 February 1998 (1998-02-26) page 2, line 8 - line 12 claims 10-13 page 4, line 1 page 7, line 14 - line 23 page 4

**Special categories of cited documents: *A* document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filling date *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filling date but	Patent family members are listed in annex. "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
later than the priority date claimed Date of the actual completion of the international search	Date of mailing of the international search report
19 December 2001	1 8. 01. 02
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Bonzano, C

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Relevant to claim No.
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Helovalit to Gailli No.
X	ASHWOOD, V. ET AL: "PD 176252 - the first high affinity non-peptide gastrin-releasing peptide (BB2) receptor antagonist" BIOORG. MED. CHEM. LETT. (1998), 8(18), 2589-2594, XP004138276 page 2589, paragraph 3 -page 2590, paragraph 1 table 3 page 2593, paragraph 3 example 6; table 1	1-3, 20-23
X	RYAN RICHARD R ET AL: "Comparative pharmacology of the nonpeptide neuromedin B receptor antagonist PD 168368." JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, vol. 290, no. 3, 1999, pages 1202-1211, XP000917708 ISSN: 0022-3565 page 1202, column 2, line 13 -page 1203, column 1, line 13 page 1210, column 1, paragraph 2	1,2, 20-24
X	TOKITA, KENJI ET AL: "Tyrosine 220 in the 5th transmembrane domain of the neuromedin B receptor is critical for the high selectivity of the peptoid antagonist PD168368" J. BIOL. CHEM. (2001), 276(1), 495-504, XP001020363 page 495, column 2, paragraph 2	1,2, 8-15, 20-24
Α	VARIOUS: "The Merck manual", BEERS AND BERKOW, N.J. XP002186135 page 988, column 1, paragraph 3 - paragraph 5	1-3, 8-15, 20-24
X	MOODY, T. W. ET AL: "Nonpeptide neuromedin B receptor antagonists inhibit the proliferation of C6 cells" EUR. J. PHARMACOL. (2000), 409(2), 133-142, XP001020329 page 133, column 1, line 1 -column 2, line 15 page 134, column 2, paragraph 3 -/	1-3, 8-15, 20-24

ategory °	citation) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
	MOODY T.W. ET AL: "Bombesin receptor antagonists." DRUGS OF THE FUTURE, (1998) 23/12 (1305-1315)., XP001020387 page 1305, column 1, paragraph 1 page 1311, column 1, line 17 - line 29	1,2, 8-15, 20-24	
	·		

Information on patent family members

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9807718	A	26-02-1998	AU BR EP JP NO PL TR WO US	733226 B2 4146697 A 9711342 A 0920424 A1 2001500850 T 990788 A 331710 A1 9900364 T2 9807718 A1 6194437 B1	06-03-1998 17-08-1999 09-06-1999 23-01-2001 19-02-1999 02-08-1999 21-05-1999 26-02-1998

/ Krosic

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For recei	10	e use only	
International Application No	CT/GB	0 0 / 0	1787
	10	MAY	2000
International Filing Date.	10	05	00
Name of receiver the large to the large transfer transfer to the large transfer tr	Kingdor ternatio	n Patent	Office lication

Applicant's or agent's file reference WARM / P22402PC (if desired) (12 characters maximum) TITLE OF INVENTION Box No. I NOVEL USES OF NON-PEPTIDE BOMBESIN RECEPTOR ANTAGONISTS Box No. II **APPLICANT** Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the This person is also inventor. address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) Warner-Lambert Company Telephone No. 201 Tabor Road Morris Plains Facsimile No. New Jersey 07950 USA Teleprinter No. State (that is, country) of nationality: State (that is, country) of residence: US US all designated This person is applicant all designated States except the United States the States indicated in the the United States of America of America only Supplemental Box for the purposes of: States Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S) Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the This person is: address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) PINNOCK, Robert Denham 3 Teasel Way applicant only Cambridge CB1 9YT applicant and inventor United Kingdom inventor only (if this check-box is marked, do not fill in below.) State (that is, country) of nationality: State (that is, country) of residence: GB This person is applicant all designated all designated States except the United States the States indicated in the for the purposes of: States the United States of America of America only Supplemental Box Further applicants and/or (further) inventors are indicated on a continuation sheet. Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE The person identified below is hereby/has been appointed to act on behalf Х agent common representative of the applicant(s) before the competent International Authorities as: Name and address: (Family name followed by given name; for a legal entity, full official Telephone No. designation. The address must include postal code and name of country.)

Bassett, Richard S (0115) 9552211 Eric Potter Clarkson Facsimile No (0115) 9552201 Park View House 58 The Ropewalk Teleprinter No. Nottingham. NG1 5DD 37540 Potter G GB Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the

34115

y

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INV	ENTOR(S)
If none of the following sub-boxes is used, this sheet should not be inclu	
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)	This person is:
PRITCHARD, Martyn Clive The Maples. 9 Bury Close St Ives	applicant only
Huntingdon Cambridgeshire PE17 4WB	X applicant and inventor
United Kingdom	inventor only (if this check-box is marked, do not fill in below.)
State (that is, country) of nationality: GB State (that is, country) of re-	sidence: GB
	nited States the States indicated in the Supplemental Box
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.) GONZALEZ, Maria Isabel	This person is:
55 Saint Barnabas Road Cambridge	applicant only
CB1 2BX United Kingdom	X applicant and inventor
	inventor only (if this check-box is marked, do not fill in below.)
State (that is, country) of nationality: ES State (that is, country) of res	sidence: GB
	nited States the States indicated in the Supplemental Box
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)	This person is:
	applicant only
	applicant and inventor
	inventor only (if this check-box is marked, do not fill in below.)
State (that is, country) of nationality: State (that is, country) of res	sidence:
	nited States the States indicated in the Supplemental Box
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)	This person is:
	applicant only
	applicant and inventor
	inventor only (if this check-box is marked, do not fill in below.)
State (that is, country) of nationality: State (that is, country) of res	sidence:
	nited States the States indicated in the Supplemental Box
Further applicants and/or (further) inventors are indicated on a continuation sheet.	

Box	No.V	DESIGNATION OF STATES									
The fo	ollowir	ng designations are hereby made under Rule 4.9(a) (ma	rk the appl	icable c	check-boxes; at least one must be marked):						
Regio	nal Pa	itent	FF		······································						
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	ΑP	ARIPO Patent: GH Ghana, GM Gambia, KE Ken	ya, LS Les	otho, M	IW Malawi, SD Sudan, SL Sierra Leone, SZ						
		Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State									
11 1		of the Harare Protocol and of the PCT									
	EA	Eurasian Patent: AM Armenia, AZ Azerbaijan, B	Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of								
		Moldova, RU Russian Federation, TJ Tajikistan, T	M Turkme	nistan a	and any other State which is a Contracting State						
		of the Eurasian Patent Convention and of the PCT	vi ranano	iiistui, u	and any other state which is a contracting state						
! X	EΡ	European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany,									
;		DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg,									
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X	OA	OAPI Patent: BF Burkina Faso, BJ Benin, CF Cer	itrai Airica	n Kepui	blic, CG Congo, CI Cote d'Ivoire, CM Cameroon,						
					nia, NE Niger, SN Senegal, TD Chad, TG Togo, and						
					ate of the PCT (if other kind of protection or treatment						
}		desired, specify on dotted line)									
Natio	nal Pa	tent (if other kind of protection or treatment desired, s	necify on a	otted liv	ne):						
	AE	United Arab Emirates	N N	_							
		1		LR	Liberia						
	AL	Albania		LS	Lesotho						
	AM	Armenia	` 🔀	LT	Lithuania						
	ΑT	Austria	, 	LU	Luxembourg						
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	ΑZ	: · Azerbaijan	X	MA	Morocco.						
	BA	Bosnia and Herzegovina		MD .	•						
		,			Republic of Moldova						
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	BG	Bulgaria	Λ	MK -	The former Yugoslav Republic of Macedonia						
	BR	Brazil									
	BY	Belarus	\mathbf{X}	MN	Mongolia						
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	CH at	nd LI Switzerland and Liechtenstein	\boxtimes	MX	Mexico						
X	CN	China	×	NO	Norway						
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X	in	India		US	United States of America						
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	KE	Kenya	1	VN	Viet Nam						
	KG	Kyrgyzstan	<u> </u> 🔯	YU	Yugoslavia						
	KР	Democratic People's Republic of Korea	! ⊠\	ZA	South Africa						
				zw	Zimbabwe						
123	KR	Republic of Korea	Check	-boxes re	served for designating States which have						
	ΚZ	Kazakhstan			o the PCT after issuance of this sheet:						
	LC	Saint Lucia	X	DZ	Algeria						
	LK	Sri Lanka	. =	AG	Antigua and Barbuda						
1 2 ΔΔ		D. C.		للدس	Antigua and Darbuda						

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

		Fo	r receiving O	ffice use only				
1.	Date of actual receipt of the purported international application:	.1 0	MAY	2000	_lo	05	00	2. Drawings:
3.	Corrected date of actual receipt due to late timely received papers or drawings compl- the purported international application:							received:
4.	Date of timely receipt of the required corrections under PCT Article 11(2):							not received:
5.	International Searching Authority (if two or more are competent): ISA	/	6. [Transmitt until sear			delayed	
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Date of receipt of the record copy by the International Bureau:

For International Bureau use only

2000

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JUNE

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Analisantis or apparis file reference	SOD FUDTHED See Notification of Trans	mittal of International Search Report
Applicant's or agent's file reference	(Form PCT/ISA/220) as v	well as, where applicable, item 5 below.
WLB0C001-PCT	ACTION	
International application No.	International filing date (day/month/year) (Ear	liest) Priority Date (day/month/year)
PCT/GB 00/04380	17/11/2000	
Applicant		
WARNER-LAMBERT COMPANY IN	C. et al.	
	the state of the second	and in transmitted to the condingant
This International Search Report has been according to Article 18. A copy is being tra	n prepared by this International Searching Authority ar ansmitted to the International Bureau.	id is transmitted to the applicant
described to the service of the serv		
This International Search Report consists	of a total of sheets.	
	a copy of each prior art document cited in this report.	
Basis of the report	•	
a. With regard to the language, the	international search was carried out on the basis of th	e international application in the
language in which it was filed, unl	less otherwise indicated under this item.	
	as carried out on the basis of a translation of the inter	national application furnished to this
Authority (Rule 23.1(b)).	the state of the s	and application, the international search
b. With regard to any nucleotide an was carried out on the basis of the	id/or amino acid sequence disclosed in the internation e sequence listing:	onal application, the international season
	onal application in written form.	
filed together with the inte	ernational application in computer readable form.	
furnished subsequently to	this Authority in written form.	
furnished subsequently to	o this Authority in computer readble form.	
the statement that the sul	bsequently furnished written sequence listing does no as filed has been furnished.	t go beyond the disclosure in the
	ormation recorded in computer readable form is identi	cal to the written sequence listing has been
furnished	·	
	ind unsearchable (See Box I).	
3. Unity of invention is lac	cking (see Box II).	-
4. With regard to the title ,		
1	ubmitted by the applicant.	
[shed by this Authority to read as follows:	
TREATMENT OF SEXUAL D	YSFUNCTION USING BOMBESIN ANTAGO	ONIST
		•
5. With regard to the abstract,		
the text is approved as si	ubmitted by the applicant.	appears in Boy III. The applicant may
the text has been established within one month from the	shed, according to Rule 38.2(b), by this Authority as it e date of mailing of this international search report, su	bmit comments to this Authority.
•	olished with the abstract is Figure No.	
1 —		None of the figures.
as suggested by the app		
because the applicant fa		
because this figure bette	r characterizes the invention.	

5771-01-MG

09/700.165

International application No. PCT/GB 00/04380

INTERNATIONAL SEARCH REPORT

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inte	ernational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. χ	Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
	Although claims1-9,11-24 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. X	Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
	see FURTHER INFORMATION sheet PCT/ISA/210
3.	Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inte	ernational Searching Authority found multiple inventions in this international application, as follows:
1.	As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
	· · · · · · · · · · · · · · · · · · ·
4.	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remar	k on Protest The additional search fees were accompanied by the applicant's protest.
· iomai	No protest accompanied the payment of additional search fees.
l	

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Present claims 1-24 relate to compounds defined by reference to a desirable characteristic or property, namely the activity as (peptide or non-peptide) bombesin receptor antagonist, with eventually affinity for the BB1 receptor, vasodilator, (modulator of) steroid hormones, neurotransmitter agonist or antagonist, hormone product usefu for the treatment of sexual dysfunctions, a monoamine synthesis modifier, a monoamine metabolism or uptake modifier useful for the treatment of sexual dysfunctions, a PDE5 inhibitor, a VIP enhancer, a compound that promotes production of NO, oestrogens, androgens. The claims cover all compounds and combinations having these characteristics or properties, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compounds for which pharmacological data have been presented in the description, and the compounds/products which are fully defined in the claims.

Claims searched completely: none. Claims searched incompletely: 1-24.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

International Application No PCT/GB 00/04380

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61K31/454 A61P15/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, BIOSIS

C. DOCUM	ENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Х	WO 00 37462 A (HORWELL DAVID CHRISTOPHER ;LEWTHWAITE RUSSELL ANDREW (GB); RAPHY J) 29 June 2000 (2000-06-29)	1-8,10
Y	claims 7,14 page 63, line 1 - line 8 page 85; example 226 page 71; example 89	11-24
Y	US 5 650 395 A (HUREL STEVEN) 22 July 1997 (1997-07-22) column 2, paragraph 3	11, 13-18, 20-24
Y	EP 1 057 829 A (JORDANIAN PHARMACEUTICAL CO. LTD.) 6 December 2000 (2000-12-06) page 2, line 5 - line 20	11, 13-18, 20-24
	page 4, line 7 - line 14 -/	

Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
Special categories of cited documents: A* document defining the general state of the art which is not considered to be of particular relevance E* earlier document but published on or after the international filing date 'L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) 'O* document referring to an oral disclosure, use, exhibition or other means 'P* document published prior to the international filing date but later than the priority date claimed	 "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
12 July 2001	19/07/2001
Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bonzano, C

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International Application No
PCT/GB 00/04380

	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	Dolovest to alaim No
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
<u>'</u>	WO 00 67708 A (ALI VASSEM ;UNIV TEXAS (US)) 16 November 2000 (2000-11-16) page 4, line 18 - line 27 page 5, line 30 - line 33	12,19
1	WO 98 07718 A (HORWELL DAVID CHRISTOPHER; PRITCHARD MARTYN CLIVE (GB); WARNER LAM) 26 February 1998 (1998-02-26) example 1 page 2, line 8 - line 12	1-24
1	ASHWOOD V ET AL: "PD 176252 - The First High Affinity Non-peptide (BB2) Receptor Antagonist" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, GB, OXFORD, vol. 8, no. 18, 22 September 1998 (1998-09-22), pages 2589-2594, XP004138276 ISSN: 0960-894X page 2589, paragraph 1 - paragraph 2 table 1	1-10
	US 5 369 094 A (SCHALLY ANDREW VICTOR ET AL) 29 November 1994 (1994-11-29) column 15, line 26 - line 35 column 1, line 37 - line 49	9
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Information on patent family members

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US 5650395	A	22-07-1997		5145196 9628214		02-10-1996 19-09-1996
EP 1057829	Α	06-12-2000	NONE			
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Information on patent family members

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